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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,694	08/25/2006	Jindrich Richter	294986US0PCT	2910

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EXAMINER
MORRIS, PATRICIA L

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
05/09/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/590,694	RICHTER ET AL.	
	Examiner	Art Unit	
	Patricia L. Morris	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,14-18 and 25-27* is/are pending in the application.

4a) Of the above claim(s) *10-13 and 19-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,14-18 and 25-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/22/06;8/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-9, 14-18 and 25-27 are under consideration in this application.

Claims 10-13 and 19-24 are held withdrawn from consideration as being drawn to nonelected subject matter 37 CFR 1.142(b).

Election/Restrictions

Applicant's election without traverse of Group I and the process of Group III in the reply filed on February 25, 2008 is acknowledged.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cazer et al. (US 6,410,520) in view of Turchetta et al. (US 2005/0215793), Brittain et al. (Polymorphism in Pharmaceutical Sciences, NY: Marcel Dekker pages 1-2, 183-226), Threifall

(Analyst, 1995, 120, 2435-2460) and Muzaffar et al. (Polymorphism and Drug Availability, J of Pharmacy (Lahore) 1979, 1(1), 59-66).

Cazer et al. teach the crystalline hydrate forms of the claimed compound . Note examples 1 and 2 therein. Brittain et al, Muzaffar et al. and Threifall. teach that compounds can exist in amorphous forms as well as in crystalline forms. Hence the claimed amorphous form as well as its relative selectivity of properties *vis-a-vis* the known compound are suggested by the references. It would appear obvious to one skilled in the art in view of the references that the instant compound would exist in different crystalline and noncrystalline forms. No unexpected or unobvious properties are noted.

Changing the form, purity or other physical characteristic of an old product does not render the new form patentable where the difference in form, purity or characteristic is inherent or rendered obvious by the prior art. In re Cofer 148 USPQ 268. Mere difference in physical property is a well known conventional variation for the same pure substance (see Brittain, p. 1-2) is prima facie obvious. Products that are merely a different form of a known compound, having the same utility as the prior art compounds, are unpatentable absent unexpected results. Ex parte Hartop, 139 USPQ 525 (Bd Pat App&Int 1963). The ex parte Hartop court held that a new crystal form of a known compound was unpatentable because the new crystal form exhibited the same utility as the known forms.

Claim Rejections - 35 USC § 112

Claims 25-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as well as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification

in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention or was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification lacks description and enablement as to whether the amorphous form is thermodynamically stable as to provide utility at room temperature for these forms in the compositions and pharmaceutical compositions. The preponderance of evidence in the state-of-the-art indicates that the pharmaceutical formulation field is well aware that amorphous forms when formulated into compositions may undergo transformation thus, the particular form may not be the same form after processing, etc, Hence, compositions containing any particular form cannot be described and enabled with specificity and particularity. For example, page 10 of the Doelker translation, states that the amorphous forms, not thermodynamically stable, in particular have a high solubility, subject to increasing the dissolution rate and the bioavailability. Further, Doelker states that amorphous novobiocine acid is transformed into crystalline form, non-resorable, in six months at ambient temperature, a phenomenon that it is possible to combat by adding methyl cellulose. The specification is silent to any specific carriers that may be employed to combat any conversion of the instant amorphous form. Muzaffar et al. on pages 63-65 (a)-(h) state that pharmaceutical preparing processes affect polymorphism. Further, Theifall on page 2452 recites that different amorphous structures may arise from different processes of production.

The enablement analysis is applied to the instant case.

The nature of the invention

The nature of the invention is the preparation of amorphous forms of the instant salt and compositions.

State and skill level of the Prior Art and predictability

Although identical in chemical composition, amorphous hydrates can have very different properties. Additionally, hydrates may dehydrate. Lester et al. teach that dehydration of hydrates may easily occur during storage or manufacturing. Amorphous forms tend to convert from less stable to more stable forms. No method exists to predict the forms of a solid compound with any significant certainty. This is why it is important to monitor the amorphous form during manufacture of the drug to see if it persists during manufacture.

The state of the pharmaceutical composition containing polymorphic form art provided per ponderous of evidence that *unless specific and particular* conditions can be obtained, the formulation process would cause polymorphic forms to change.

See :

--Muzaffar et al. p.63-65 (a)-(h) state that pharmaceutical preparing processes affect polymorphism;

--Theifall on. p.2452 recites that different amorphous structures may arise from different processes of production;

--Doelker et al. abstract "...a given drug, although chem. well defined, may exhibits quite different behavior. Process conditions (grinding, tableting, granulations, drying) may also affect secondary properties of the drug, such as compactibility, wetttability, solvent, dissolution rate, bioavailability and even pharmacological, activity."

--Xu ...Influences of environmental conditions such as temperature, humidity, phase transition can cause amorphous materials to transform into crystals during storage and transportation.

--Singhal et al. "..It should be pointed out that a major portion of any formulation effort is the choice of exipients and processes which minimize the chemical instability of the drug…." P.338, left col.

The amount of direction or guidance and the presence or absence of working examples

Figure 4 of the specification only disclose the X-ray diffraction pattern of one compound, i.e., risedronate sodium hydrate in the amorphous form rather than the compositions being claimed in terms of the specific X-ray diffraction patterns. Hydrates often change into other forms during drug manufacture into a pharmaceutical composition. Based on the unpredictability in the art, the applicant is not entitled to the X-ray diffraction patterns claimed for the pharmaceutical compositions.

As evidenced by the art of record, it is well known that amorphous forms can convert to other forms. Appellants have failed to show that the claimed amorphous hydrate and not some other form actually treats any disease.

The breadth of the claims

The breadth of the claims are drawn to the specific amorphous hydrate forms and in addition to the pharmaceutical compositions.

The quantity of experimentation needed

The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to the pharmaceuticals compositions being claimed and verifying that they have the specific X-ray diffraction patterns being claimed which are not disclosed in the specification.

In terms of the 8 Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of unpredictability in the art of the invention, and the poor amount of direction provided by

applicants. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 14-18 and 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites that the instant salt is an amorphous form only and yet the compound shows two sharp peaks which indicates that salt is not an amorphous form.

Any X-ray diffraction of an amorphous material is only to show no diffraction or non-crystalline, *i.e.,* a single broad, shallow peak termed an *amorphous halo*. Note pages 578-579 of Nerurkar et al.

No antecedent basis can be found for the term substance in claims 2-9, 14-18 and 25-27. Further, the term is indefinite to its meaning.

Claim 15 violates 35 U.S.C. 101 and 35 U.S.C. 112, since it is drafted in terms of use. See Clinical Products vs. Brenner, 255 F. Supp. 151; 149 USPQ 475 (D.C. District of Columbia 1966).

The claims measure the invention. United Carbon Co. V. Binney & Smith Co., 55 USPQ 381 at 384, col. 1, end of 1st paragraph, Supreme Court of the United States (1942).

The C.C.P.A. in 1978 held "that invention is the subject matter defined by the claims submitted by the applicant. We have consistently held that no applicant should have limitations

of the specification read into a claim where no express statement of the limitation is included in the claim": In re Priest, 199 USPQ 11, at 15.

Conclusion

Claims 1-9, 14-18 and 25-27 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia L. Morris whose telephone number is (571) 272-0688. The examiner can normally be reached on Mondays through Fridays.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Patricia L. Morris/
Primary Examiner, Art Unit 1625

plm
May 1, 2008